

REMARKS

Claims 1-18 are currently pending. The specification has been amended at page 6, line 13 to correct a spelling error for “3-hydroxytyramine.” Claim 6 has been amended to add a period. Claims 4 and 9 have been amended to correct the spelling of “3-hydroxytyramine.”

Applicants note the Examiner’s comments with regard to the IDS. A supplemental information disclosure statement is being filed concurrently herewith along with a copy of the nonpatent literature reference. Pages numbers and the correct date are listed in the IDS.

Applicants further note the Examiner’s statement that claims 4, 5, 9 and 10 are not supported in the prior art, that is that there is no art cited against these claims. Thus these dependent claims would be allowable if rewritten in independent form.

35 U.S.C. § 103

Claims 1-3, 6-8 and 11-18 stand rejected as obvious over Archer in view of Duatti because, *inter alia*, it would have been obvious to substitute the tridentate diphosphine ligands and bidentate electron-donating ligands of Duatti onto the Tc=NR complexes of Archer to generate a single isomer that is site-specific to the desired location of the body of a patient for improved radiodiagnostic imaging and radiotherapy.

At the outset, applicants point out that in order to establish a *prima facie* case of obviousness, there must be some suggestion or motivation in the cited references to modify the reference or to combine reference teachings to obtain Applicant’s claimed invention and there must be a reasonable expectation of success. MPEP § 2143.

For the reasons discussed below, applicants respectfully submit that the proposed modification fails to meet at least the above-mentioned criteria and thus fails to establish a *prima facie* case of obviousness.

Applicants point out that Archer merely discloses the preparation of Tc imido radiopharmaceutical complexes where L_n is a mono or multi-dentate ligand such as: phosphines and arsines of the general formula Q₂B(CD₂)_nBQ₂; MDP; TU; TMA; DMSA; GLUC; EHDP; DTPA; HIDA; EHIDA; PIPIDA; Dialkyl dithiocarbamate, Isonitirles of the general type C≡NR₄, R₄=alkyl, alkoxy, ether; BAT derivatives; phenanthroline; pentane-2,4-dione; bipyridyl; propylene amine oxime backbone ligands and bisthiosemicarbazones as shown at col. 5, lns 1-5. However, even if Archer describes metal-imido complexes containing a multidentate ligand, it does not suggest the specific replacement of the monodentate phosphine donors in the compounds of formula [Tc(NR)C₁₃(PPh₃)₂] with a tridentate ligand and the addition of bidentate ligands in order to improve the stability of Tc-imido complexes.

Duatti describes a radioactive transition metal nitride heterocomplex and describes that metal nitrides are characterized by a triple bond, not a double bond. (col. 2 lns. 38-41). Thus metal nitrides are totally different from ionic imido metal compounds. While Duatti does describe bidentate ligands such as ethylenediamine and tridentate ligands, such as at col. 3 lns 3-4, which coordinate with metal nitrides, nowhere does Duatti teach or suggest that such ligands could successfully coordinate with imido-metals.

Thus, neither Archer, nor Duatti, teach or suggest that Duatti's bidentate and tridentate ligands would even be able to coordinate with a metal-imido complex. Therefore, the person of ordinary skill in the art aimed at developing an improved, site-specific imido

compound for radiodagnostic imaging and radiotherapy would not have had any motivation to modify the compounds of Archer with the bidentate and tridentate ligands of Duatti.

Additionally, the present specification makes clear that all previous attempts to replace the monodentate P-donors in compound [Tc(NPh)Cl₃(PPh₃)₂] with various polydentate chelates were not successful, thus the prior art taught that the imido group should be stabilized only by the presence of monodentate monophosphine ligands. (Specification at pp. 3-4). This is not surprising given that the coordination chemistry of ligands, such as Duatti's, which are able to form a stable metal nitride coordinated complex, would not have been expected by one of ordinary skill in the art to be able to form a stable and geometrically defined metal-imido coordinated complex. This is so because Duatti, for example, states explicitly that Y is a bidentate ligand (col. 2 lns. 7-11) and that Y is "chosen so as to coordinate with the core of the metal nitride having a M≡N bond and form an unsymmetrical tbp geometry to stabilize the complex, without producing an optical isomer or a geometrical isomer in the coordination."

Thus one of ordinary skill in the art would not have had any reasonable expectation of success in modifying Archer with the bidentate and tridentate ligands of Duatti.

Furthermore, applicants note the surprising result achieved by using imido metal compounds coordinated with bidentate and tridentate ligands, namely the ability to perform reactions on a microscopic scale (*i.e.*reactions occurring at concentrations of 10⁻⁶ to 10⁻⁹ M with microgram to nanogram amounts of ⁹⁹Tc as is desired by hospital labs), which is provided by applicant's claimed invention, and that neither Archer nor Duatti teach or suggest that using a tridentate ligand and a bidentate ligand would achieve this surprising result. (See specification at p. 1-2 bridging par.).

Therefore, for the above reasons, claims 1-3, 6-8, and 11-18 are not obvious over Archer in view of Duatti. Thus, applicants respectfully request withdrawal of the § 103 rejection and the speedy issuance of a notice of allowance.

CONCLUSION

If a telephone interview would be of assistance in the prosecution of this application, the Examiner is invited to telephone Applicants' undersigned attorneys at his convenience at the number provided below.

No fees are believed due in connection with the filing of this *Amendment and Response*. However, the Director is hereby authorized to charge any required fees and credit any overpayments to Deposit Account No. 50-0540.

Respectfully submitted,

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